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PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * SESSION RESUMED IN FILE 'HCAPLUS' AT 12:54:42 ON 10 AUG 2006 FILE 'HCAPLUS' ENTERED AT 12:54:42 ON 10 AUG 2006 COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 370.35	TOTAL SESSION 705.76
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE	SINCE FILE ENTRY -52.50	TOTAL SESSION -52.50
=> file reg COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 372.88	TOTAL SESSION 708.29
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE	SINCE FILE ENTRY -52.50	TOTAL SESSION -52.50

FILE 'REGISTRY' ENTERED AT 12:55:04 ON 10 AUG 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES: 9 AUG 2006 HIGHEST RN 900096-56-2 DICTIONARY FILE UPDATES: 9 AUG 2006 HIGHEST RN 900096-56-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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http://www.cas.org/ONLINE/UG/regprops.html

Uploading C:\Program Files\Stnexp\Queries\10535187a.str

chain nodes :

10 .11 12 13 14 15 16 17 18 19 20 21 22 23

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

8-10 9-11 11-12 11-13 12-14 12-19 14-15 15-16 15-20 16-17 17-18 20-21

20-22 21-23

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 9-11 11-13 12-14 14-15 20-21

20-22

exact bonds :

8-10 11-12 12-19 15-16 15-20 16-17 17-18 21-23

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS

L10 STRUCTURE UPLOADED

=> d 110 L10 HAS NO ANSWERS L10 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 110

SAMPLE SEARCH INITIATED 12:55:31 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 320 TO ITERATE

100.0% PROCESSED 320 ITERATIONS 7 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 5327 TO 7473
PROJECTED ANSWERS: 7 TO 298

L11 7 SEA SSS SAM L10

=> s 110 full

FULL SEARCH INITIATED 12:55:39 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 6180 TO ITERATE

100.0% PROCESSED 6180 ITERATIONS 118 ANSWERS

SEARCH TIME: 00.00.01

L12 118 SEA SSS FUL L10

=> file hcaplus

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
166.94
875.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE 0.00 -52.50

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FILE COVERS 1907 - 10 Aug 2006 VOL 145 ISS 7 FILE LAST UPDATED: 9 Aug 2006 (20060809/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

1 L12/P AND HYDRATE? L13

=> d ed abs ibib hitstr 1

ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN L13

Entered STN: 13 Jul 1986 ED

GT

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I, II, X = Cl, CF3; Y = (CH2)aCHONR5 or (CH2)bNR5CO; Z = (CH2)bCONR5 or (CH2)cNR5CO; B = Q-Q4; R1 = H, alkyl; R2, R5 = H, alkyl, Ph, phenylalkyl; R3, R4 = H, (substituted) alkyl, Ph or R3R4 may form a ring; R6, R8 = OH, (substituted) alkoxy, etc.; R7 = H, (substituted) alkyl; a = 0-8; b = 1-8; c = 2-8; m = 1-4; n = 0, 1; p, q = 1, 0, 2] and their pharmaceutically acceptable salts, useful as antihypertensives (no data), were prepared Thus, (2S)-[(benzyloxy)carbonyl]-S,S-perhydroindole was acylated with N-[(5S)-(ethoxycarbonyl)-5-(1S-carboxyethylamino)pentyl]-6-chloro-3,4-dihydro-1,1-dioxo-7-sulfamoyl-1,2,4-benzothiadiazin-3yl]acetamide hydrochloride in DMF containing N-hydroxybenzotriazole hydrate and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide-HCl at. 0° to give, after deprotection of the intermediate, 1-[N-[(1S)-(ethoxycarbonyl)-5-[2-(6-chloro-3,4-dihydro-1,1-dioxo-7sulfamoyl-1,2,4-benzothiadiazin-3-yl)acetamido]pentyl]-(S)-alanyl]-cis,synoctahydroindole-(2S)-carboxylic acid. The prepared compds. are useful for treatment of congestive heart failure and glaucoma and had diuretic activity (no data).

ACCESSION NUMBER: 1986:406825 HCAPLUS

DOCUMENT NUMBER: 105:6825

TITLE: Benzothiadiazinyl and quinazolinyl substituted

carboxylalkyl dipeptides useful as antihypertensive

INVENTOR(S): Neustadt, Bernard R.; Andrews, David R.; McNamara,

Paul E.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE:

U.S., 12 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4559340	Α	19851217	US 1983-555311	19831125
US 4616012	Α	19861007	US 1985-797104	19851112
US 4778795	Α	19881018	US 1986-903545	19860903
US 4906635	Α	19900306	US 1988-220183	19880718
US 5017567	A	19910521	US 1990-460425	19900103
PRIORITY APPLN. INFO.:			US 1983-555311 A	2 19831125
			US 1985-797104 A	3 19851111
			US 1986-903545 A	3 19860903
			US 1988-220183 A	3 19880718

102605-78-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of)

RN 102605-78-7 HCAPLUS

•x HBr

IT 102605-60-7P 102605-62-9P 102743-99-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as antihypertensive)

RN 102605-60-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]acetyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

C1
$$H_2N-S$$
 NH $CH_2-C-NH-(CH_2)_4-CH-NH-CH-C=0 H_2N-S $H_2N-$$

RN 102605-62-9 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]acetyl]amino]-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, hydrochloride (9CI) (CA INDEX NAME)

•x HCl

RN 102743-99-7 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-2-yl]acetyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

=> s l12/p and salt? 70 L12/P 1166384 SALT? L14 35 L12/P AND SALT?

=> d ed abs ibib hitstr 1-35

L14 ANSWER 1 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 14 Jul 2006

AB The invention relates perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] aralkyl ester salts used in the synthesis of perindopril. Thus, (2S, 3aS, 7aS) -octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

ACCESSION NUMBER: 2006:680403 HCAPLUS

DOCUMENT NUMBER: 145:124844

TITLE: Process for the synthesis of (2S, 3aS, 7aS) -1-(S) -

alanyloctahydro-1H-indole-2-carboxylic acid

derivatives and use in the synthesis of perindopril INVENTOR (S): Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Gunjal, Sanjay Tukaram; Panda, Nalinakshya

Balaram; Jadhav, Dilip Uttam

PATENT ASSIGNEE(S): IPCA Laboratories Limited, India

SOURCE: Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. ---------**----**-----EP 1679072 A1 20060712 EP 2005-113099 20051230 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

PRIORITY APPLN. INFO.: IN 2005-MU17 A 20050106

107133-36-8P, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(process for synthesis of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT: 6 THERE ARE

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 07 Jul 2006

AB A process for preparing perindopril erbumine, useful in the treatment of hypertension, comprises reacting an active ester of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanine with an organic salt of perhydroindole-2-carboxylic acid, followed by the addition of tert-butylamine. An example using the acetonoxime as active ester in acetonitrile in the presence of phosphacene afforded 90% perindopril erbumine (99.5% purity).

ACCESSION NUMBER: 2006:655550 HCAPLUS

DOCUMENT NUMBER: 145:83667

TITLE: Process for preparing perindopril erbumine INVENTOR(S): Palomo Nicolau, Francisco; De Leon, Dorcas

PATENT ASSIGNEE(S): Quimica Sintetica, S.A., Spain

SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	NO.			KIN	D :	DATE		į	APPL	ICAT	ION I	NO.		D	ATE	
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WO 2006	0702	76		A1		2006	0706	1	WO 2	005-	IB39	28		2	0051	215
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	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KM,	KN,	ΚP,	KR,
	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	MX,
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	SG,	SK,	SL,	SM,	SY,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,

VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM ES 2255872 20060701 A1 ES 2004-3168 20041231 PRIORITY APPLN. INFO.: ES 2004-3168 20041231 107133-36-8P, Perindopril erbumine RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of perindopril erbumine) RN107133-36-8 HCAPLUS CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME) CM 1 CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

3

ED Entered STN: 16 Dec 2005

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed

by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

ACCESSION NUMBER: 2005:1311320 HCAPLUS

DOCUMENT NUMBER: 144:7101

TITLE: Method for synthesis of perindopril and its

pharmaceutically acceptable salts

INVENTOR (S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PATENT ASSIGNEE(S): Adir et Compagnie, Fr. SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent French

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.								APPLICATION NO.								
	1367	063			A 1			1203		EP 2	003-	2919	31		2		
							RO,										ΙΙ,
ΑU	2004																729
	2533						2005										
WO	2005	0123	33		A2												
WO	2005	0123	33		A3		2005	0324									
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OTHER SO	OURCE	(S):			MARI	PAT	144:	7101	1	WO 2	004-1	FR20	35	ı	W 20	0040	729

IT 82834-16-0P 107133-36-8P

> RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN82834-16-0 HCAPLUS

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-CN (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 Dec 2005

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or

trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

ACCESSION NUMBER: 2005:1311047 HCAPLUS

DOCUMENT NUMBER: 144:7100

TITLE: Method for synthesis of perindopril and its

pharmaceutically acceptable salts

INVENTOR(S): Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal

PATENT ASSIGNEE(S): Adir et Compagnie, Fr. SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                                         APPLICATION NO.
                        KIND
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                                                                 DATE
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                               20031203 EP 2003-291930
     EP 1367062
                        A1
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     AU 2004261440
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                               20050210
                                        AU 2004-261440
                                                                 20040729
                                          WO 2004-FR2036
     WO 2005012328
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                               20050210
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    WO 2005012328
                         A3
                               20050324
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            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
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            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
PRIORITY APPLN. INFO.:
                                           EP 2003-291930
                                                              A 20030731
                                           WO 2004-FR2036
                                                              W 20040729
OTHER SOURCE(S):
                        CASREACT 144:7100; MARPAT 144:7100
     82834-16-0P, Perindopril 107133-36-8P, Perindopril
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (synthesis of perindopril from hexahydroindolecarboxylate and
       bromopropionyl chloride)
RN
     82834-16-0 HCAPLUS
CN
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
```

Absolute stereochemistry. Rotation (-).

(CA INDEX NAME)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1 -

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

- THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L14 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
- ED Entered STN: 02 Dec 2005
- AB The invention relates to a process for the preparation of the ACE inhibitor perindopril, its pharmaceutically-acceptable salts and intermediates obtained in the process. The process involves conversion of N-[(1S)-1-carbethoxybutyl]-L-alanine to the acid chloride hydrochloride

and reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or a an ester or salt. The examples describe the synthesis of perindopril erbumine by reactions carried out in CH2Cl2.

ACCESSION NUMBER:

2005:1262577 HCAPLUS

DOCUMENT NUMBER:

144:7098

TITLE:

Process for the preparation of perindopril and its

salts

INVENTOR (S): PATENT ASSIGNEE(S): Merslavic, Marjo; Smid, Janja; Tomsic, Zdenka Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia

SOURCE:

PCT Int. Appl., 19 pp.

CODEN: PIXXD2 Patent

DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

											APPLICATION NO.					DATE		
	WO	2005	1135	00													0050	510
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			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KM,	ΚP,	KR,	ΚZ,
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								TN,										
			ZA,	ZM,	ZW													
		RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,
			AZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,
								BF,										
			MR,	NE,	SN,	TD,	TG											
	SI	2180	0			C		2005	1231		SI 20	004-	143			20	040	514
	SI	2185	2			C	;	2006	0228		SI 20	004-2	235			20	040	305
PRIO	RITY	APP	LN.	INFO	. :						SI 20	004-	143		1	A 20	040	514
											SI 20	004-2	235		1	A 20	0040	305
OTHE	R SC	URCE	(S):			CAS	REAC'	T 14	4:70	98; 1	MARP	AT 1	44:70	98				
IT	828	34-1	6-0P	, Pe	rind	opri	1 10	7133	-36-8	8P, 3	Peri	ndop	ril					
	erk	umin	e 86	9954	-04-	1P 8	6995	4-08	-5P			_						
	869	954-	09-6	P														
	RL:	IMF	(In	dust	rial	man	ufac	ture); SI	PN (Syntl	heti	c pre	epara	ation	n);]	PREP	
	(Pr	epar	atio	n)							_		_					
		(pro	cess	for	pre	para	tion	of p	peri	ndop:	ril a	and :	its :	salt	s)			
RN	828	34-1								-								
CN	1H-	Indo	le-2	-carl	ооху	lic a	acid	, 1-	[(2S)	-2-	[[(18	S) -1	_					
														, (2	S,3a9	S,7a9	3) -	(9CI)
	(CA	IND	EX N	AME)					_			_						

Absolute stereochemistry. Rotation (-).

```
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.
with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5
```

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

RN 869954-04-1 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monopotassium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

K

RN 869954-08-5 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monolithium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

● Li

RN 869954-09-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monosodium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Na

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

2

ED Entered STN: 19 Oct 2005

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy- or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBT, followed by catalytic hydrolgenolysis. The starting ester was obtained from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1 was obtained from norvaline Et ester and pyruvic acid under catalytic hydrogenation conditions. The method was applied to the synthesis perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl ester and 21.26 g 1).

ACCESSION NUMBER:

2005:1117891 HCAPLUS

DOCUMENT NUMBER:

143:367597

TITLE: INVENTOR(S): Process for the preparation of perindopril Kankan, Rajendra Narayanrao; Rao, Dharmaraj

Ramachandra

PATENT ASSIGNEE(S):

SOURCE:

Neopharma Limited, UK

Brit. UK Pat. Appl., 21 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2413128	A1	20051019	GB 2004-8258	20040413
WO 2005100317	A1	20051027	WO 2005-GB1355	20050407
W: AE, AG, A	L, AM, AT	, AU, AZ,	BA, BB, BG, BR, BW, BY,	BZ, CA, CH,
CN, CO, C	R, CU, CZ	, DE, DK,	DM, DZ, EC, EE, EG, ES,	FI, GB, GD,
GE, GH, G	M, HR, HU	, ID, IL,	IN, IS, JP, KE, KG, KM,	KP, KR, KZ,
LC, LK, L	R, LS, LT	, LU, LV,	MA, MD, MG, MK, MN, MW,	MX, MZ, NA,
NI, NO, N	Z, OM, PG	, PH, PL,	PT, RO, RU, SC, SD, SE,	SG, SK, SL,
SM, SY, T	J, TM, TN	, TR, TT,	TZ, UA, UG, US, UZ, VC,	VN, YU, ZA,
ZM, ZW				
RW: BW, GH, G	M, KE, LS	, MW, MZ,	NA, SD, SL, SZ, TZ, UG,	ZM, ZW, AM,
AZ, BY, K	G, KZ, MD	, RU, TJ,	TM, AT, BE, BG, CH, CY,	CZ, DE, DK,
EE, ES, F	I, FR, GB	, GR, HU,	IE, IS, IT, LT, LU, MC,	NL, PL, PT,
RO, SE, S	I, SK, TR	, BF, BJ,	CF, CG, CI, CM, GA, GN,	GQ, GW, ML,

MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2004-8258 A 20040413

OTHER SOURCE(S): MARPAT 143:367597

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril

erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

(preparation of perindopril by acylation of octahydroindolecarboxylates with ethoxycarbonylbutylalanine)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9

CMF C4 H11 N

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NH<sub>2</sub>
|
H<sub>3</sub>C-C-CH<sub>3</sub>
|
CH<sub>3</sub>
```

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 29 Jul 2005

AB Complexes of the ACE-inhibitor perindopril, a salt, an addition salt or a derivative thereof with cyclodextrins, polyvinylpyrrolidone or hydroxypropyl cellulose, and processes for their preparation are described. E.g., complexes of perindopril erbumine with β -cyclodextrin and Me

and hydroxypropyl β-cyclodextrins were prepared

ACCESSION NUMBER:

2005:673315 HCAPLUS

DOCUMENT NUMBER:

143:159626

TITLE:

Inclusion complexes of perindopril

INVENTOR(S):

Rucman, Rudolf

PATENT ASSIGNEE(S):

LEK Pharmaceuticals D.D., Slovenia

SOURCE:

PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                        KIND DATE
                                         APPLICATION NO.
                                                                DATE
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                              -----
                                          -----
     WO 2005068490
                        A1 20050728 WO 2005-EP282
                                                                20050113
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
            RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
            MR, NE, SN, TD, TG
                               20050831
    SI 21703
                        C
                                          SI 2004-11
                                                                 20040114
PRIORITY APPLN. INFO.:
                                          SI 2004-11
                                                              A 20040114
    107133-36-8DP, Perindopril erbumine, compds., with hydroxypropyl
    and Me cyclodextrins 860260-85-1P 860260-86-2P
     860260-87-3P 860260-88-4P 860260-89-5P
    RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (inclusion complexes of perindopril)
RN
     107133-36-8 HCAPLUS
CN
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.
    with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)
    CM
         1
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Young, Shawquia, Page 19

CRN 82834-16-0

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10/08/2006,10535187e.trn
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CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

$$^{\mathrm{NH_2}}_{|}_{|}_{\mathrm{H_3C-C-CH_3}}_{|}_{|}_{\mathrm{CH_3}}$$

RN 860260-85-1 HCAPLUS
CN β-Cyclodextrin, compd. with 2-methyl-2-propanamine
(2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 7585-39-9 CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

CM 2

CRN 107133-36-8

CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0

CMF C19 H32 N2 O5

CM 4

CRN 75-64-9 CMF C4 H11 N

RN 860260-86-2 HCAPLUS

CN γ-Cyclodextrin, compd. with 2-methyl-2-propanamine (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 17465-86-0 CMF C48 H80 O40

CM 2

CRN 107133-36-8 CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 4

CRN 75-64-9 CMF C4 H11 N

RN 860260-87-3 HCAPLUS

CN \(\varepsilon \)-Cyclodextrin, compd. with 2-methyl-2-propanamine \((2S, 3aS, 7aS) - 1 - [(2S) - 2 - [[(1S) - 1 - (ethoxycarbonyl) butyl] amino] - 1 - oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 156510-98-4 CMF C60 H100 O50

Absolute stereochemistry.

CM 2

CRN 107133-36-8

CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0

CMF C19 H32 N2 O5

CM 4

CRN 75-64-9 CMF C4 H11 N

RN 860260-88-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 1-ethenyl-2-pyrrolidinone homopolymer and 2-methyl-2-propanamine (1:?:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107133-36-8

CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 3

CRN 75-64-9 CMF C4 H11 N

CM 4

CRN 9003-39-8 CMF (C6 H9 N O)x CCI PMS

CM 5

CRN 88-12-0 CMF C6 H9 N O

RN 860260-89-5 HCAPLUS
CN Cellulose, 2-hydroxypropyl ether, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-

[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and 2-methyl-2-propanamine (?:1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107133-36-8 CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0 CMF C19 H32 N2 O5

CM 3

CRN 75-64-9 CMF C4 H11 N

NH₂ | H₃C-C-CH₃ | CH₃

CM 4

CRN 9004-64-2 CMF C3 H8 O2 . x Unspecified

CM 5

CRN 9004-34-6 CMF Unspecified CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 6

CRN 57-55-6 CMF C3 H8 O2

ОН | Н3С-СН-СН2-ОН

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

5

ED Entered STN: 24 May 2005

The dipeptide, (I, R30CO-CHR1NHCHR2CONR4R5 wherein R1 = Pr or phenethyl; R2 = Me, 4-trifluoroacetamidobutyl, or 4-aminobutyl; and R3 = H or ethyl), is prepared by allowing to react R30COCHR1NHCHR2COOH with bis(trichloromethyl) carbonate in solvent at (-20)-100°C for 1-50 h to obtain N-carboxylic anhydride and then coupling with alpha-amino acid or its derivative in organic solvent at (-20)-100°C for 1-50 h. The alpha-amino acid or its derivative, R4R5NH, is 1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid benzyl ester, 2-azabicyclo[3.3.0]octane-3-carboxylic acid, 2-pyrrolidinecarboxylic acid, or octahydro-1H-indole-2-carboxylic acid.

ACCESSION NUMBER:

2005:436413 HCAPLUS

DOCUMENT NUMBER:

143:139085

TITLE:

Method for preparing N-carboxyalkyl dipeptide type

angiotensin converting enzyme inhibitor

INVENTOR(S):

Shi, Huilin; Zhang, Qingwen; Zhong, Jingfen; Shan,

Xiaoyan; Chen, Guoliang; Zhou, Minghua

PATENT ASSIGNEE(S): Shanghai Research Institute of Pharmaceutical

Industry, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

CN 1429835 A 20030716 CN 2002-139936 20021230
PRIORITY APPLN. INFO.: CN 2002-139936 20021230

IT 82834-16-0P, Perindopril

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tert-butylamine salt; method for preparing N-carboxyalkyl dipeptide type angiotensin converting enzyme inhibitor)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 29 Apr 2005

AB Crystalline perindopril erbumine (I.H2NBu-tert) is prepared and the x-ray (powder) diffraction pattern given. The process comprises reacting a

solution of perindopril (I), in a solvent selected from DMF or di-Me acetals of lower aliphatic aldehydes and ketones with tertiary butylamine and crystallization

of the erbumine salt thus obtained by heating the reaction mixture to reflux, filtering hot, cooling gradually to 20-30°, and further cooling to 0-15° for 30 min-1 h and finally filtering off and drying the crystals.

ACCESSION NUMBER: 2005:371219 HCAPLUS

DOCUMENT NUMBER: 142:435775

TITLE: Novel method for preparation of crystalline

perindopril erbumine

INVENTOR(S): Singh, Girij Pal; Godbole, Himanshu Madhav; Nehate,

Sagar Purushottam Lupin Ltd., India

PATENT ASSIGNEE(S): Lupin Ltd., India SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
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                         ----
                               -----
                                           -----
     WO 2005037788
                         A1
                               20050428
                                          WO 2003-IN340
                                                                  20031021
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
            LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2003300689
                               20050505
                         A1
                                         AU 2003-300689
                                                                  20031021
    EP 1675827
                                          EP 2003-818870
                         A1
                               20060705
                                                                  20031021
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.:
                                           WO 2003-IN340
                                                               A 20031021
    82834-16-0P, Perindopril
    RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (preparation of crystalline perindopril erbumine)
RN
     82834-16-0 HCAPLUS
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
CN
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (25,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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IT 107133-36-8P, Perindopril erbumine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of crystalline perindopril erbumine)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 04 Mar 2005

GT

Pure perindopril tert-butylamine salt is obtained by extracting an AB aqueous solution of perindopril (I), namely (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid, or its salt contaminated with impurities with a suitable organic solvent such as methylene dichloride at a pH of 4.0 to 6.5, separating

the

organic layer, isolating I from the organic layer and converting it into tert-butylamine salt. Thus, perindopril tert-butylamine salt (15 q, purity 92.4%) was added to water (100 mL) and CH2Cl2 (100 mL) and the pH of the mass was adjusted to 5.4 by using 20% dilute HCl. The phases were separated and the aqueous layer was washed with CH2Cl2 (2 x 75 mL). The CH2Cl2 layer and washings are combined and the combined organic phase was washed with water (50 mL) and then with 10% aqueous NaCl (50 mL). The organic layer was dried over Na2SO4 and concentrated to give a residue, perindopril, (99.3 % purity). EtOAc (255 mL) was added to the residue (15 g) and stirred for 10 min to obtain a clear solution Tert-Butylamine was added dropwise to the solution at 30° and stirred for 1 h at the same temperature The reaction mass was then heated to reflux, passed over hiflo rapidly at reflux temperature and washed with hot EtOAc (30 mL). Then, the reaction mass was stirred for 2 h at .apprx.30°, cooled to 0°, and stirred for further 2 h at 0° to 5°. The separated solid was filtered, washed with EtOAc (15 mL), and dried to give 12

g of 99.77% pure perindopril tert-butylamine salt. ACCESSION NUMBER: 2005:182626 HCAPLUS

DOCUMENT NUMBER:

142:280052

TITLE:

Process for pure perindopril tert-butylamine

salt

INVENTOR(S):

Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura;

Raji Reddy, Rapolu; Muralidhara Reddy, Dasari;

Ramakrishna Reddy, Matta

PATENT ASSIGNEE(S):

Hetero Drugs Limited, India

SOURCE:

PCT Int. Appl., 15 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE					APPLICATION NO. DATE											
WO 2005019173				A1 20050303			WO 2003-IN276						20030821			
WO 2005	OTST	13		ΑT		2005	0303		WU Z	003-	TM2 /	0		۷.	2020	92 I
₩:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,	TN,
	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW			
RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003263584 20050310 AU 2003-263584 A1 20030821 PRIORITY APPLN. INFO.: WO 2003-IN276 A 20030821 82834-16-0P, Perindopril RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; process for pure perindopril tert-butylamine salt) RN · 82834-16-0 HCAPLUS 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-CN(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 Nov 2004

AB A process for the preparation of the ACE inhibitor perindopril involves activation of N-[1(S)-(ethoxycarbonyl)butyl]-(S)-alanine (1) with a tetramethyluronium salt in the presence of a tertiary organic base, coupling with (2S, 3aS, 7aS) -octahydroindole-2-carboxylic acid (2) or an ester, and deprotection. Thus, a mixture of 1, 2 benzyl ester, TBTU and diisopropylethylamine in DMF/CH2Cl2 was stirred for 4 h to afford benzyl-perindopril, which was converted to perindopril by phase transfer or classical hydrogenation.

ACCESSION NUMBER:

2004:996205 HCAPLUS

DOCUMENT NUMBER:

141:395815

TITLE:

A process for the preparation of perindopril using

tetramethyluronium salts as coupling

reagents

INVENTOR(S):

Rucman, Rudolf

PATENT ASSIGNEE(S):

Lek Pharmaceuticals D.D., Slovenia

SOURCE:

PCT Int. Appl., 15 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE				
WO 2004099236		WO 2004-SI20	20040507				
		BA, BB, BG, BR, BW,					
		DM, DZ, EC, EE, EG,					
		IN, IS, JP, KE, KG,					
		MD, MG, MK, MN, MW,					
		RO, RU, SC, SD, SE,					
		UG, US, UZ, VC, VN,					
		NA, SD, SL, SZ, TZ,					
		TM, AT, BE, BG, CH,					
		IE, IT, LU, MC, NL,					
SN, TD, TG	Br, Bo, Cr, CG,	CI, CM, GA, GN, GQ,	GW, ML, MR, NE,				
	C 20041221	GT 2002 110	,				
51 21506	20041231	SI 2003-118	20030508				
		EP 2004-731809					
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,				
IE, SI, FI,	RO, CY, TR, BG,	CZ, EE, HU, PL, SK					
PRIORITY APPLN. INFO.:		SI 2003-118	A 20030508				
		WO 2004-SI20					
OTHER SOURCE(S):	CASREACT 141:39	CASREACT 141:395815; MARPAT 141:395815					
IT 82834-16-0P, Perind			_				

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril using tetramethyluronium salts as coupling reagents)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

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NH<sub>2</sub>
|
H<sub>3</sub>C-C-CH<sub>3</sub>
|
CH<sub>3</sub>
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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 Nov 2004

AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises esterifying (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) with benzyl alc. (or the 4-chloro or 4-alkoxy derivative) in the presence of benzenesulfonic acid as catalyst, treating the intermediate ester benzenesulfonate with N-[(S)-1-carbethoxybutyl]-L-alanine (II), and ester cleavage. Thus, I benzyl ester benzenesulfonate (40 g) was prepared, its suspension in CH2Cl2 made alkaline with aqueous ammonia,

and the organic layer separated Treatment with II at 10-15 $^{\circ}$ C in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide and workup afforded 43 g perindopril benzyl ester.

ACCESSION NUMBER:

2004:996123 HCAPLUS

DOCUMENT NUMBER:

141:411226

TITLE:

Process for preparation of perindopril and its

salts

INVENTOR(S):

Kankan, Rajendra Narayanrao; Rao, Dharmaraj

Ramachandra

PATENT ASSIGNEE(S):

Cipla Limited, India; Wain, Christopher Paul

SOURCE:

PCT Int. Appl., 26 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	NO.	KIND DAT		PLICATION NO.				
WO 2004			11118 WO	2004-GB2029				
W :	AE, AG, AL, CN, CO, CR, GE, GH, GM, LK, LR, LS, NO, NZ, OM, TJ, TM, TN, BW, GH, GM, AZ, BY, KG, EE, ES, FI, SI, SK, TR,	AM, AT, AU CU, CZ, DE HR, HU, ID LT, LU, LV PG, PH, PL TR, TT, TZ KE, LS, MW KZ, MD, RU FR, GB, GR	, AZ, BA, B , DK, DM, D , IL, IN, I , MA, MD, M , PT, RO, R , UA, UG, U , MZ, NA, S , TJ, TM, A , HU, IE, I	Z, EC, EE, EG, S, JP, KE, KG, G, MK, MN, MW, U, SC, SD, SE, S, UZ, VC, VN, D, SL, SZ, TZ, T, BE, BG, CH, T, LU, MC, NL,	BY, BZ, CA, CH, ES, FI, GB, GD, KP, KR, KZ, LC, MX, MZ, NA, NI, SG, SK, SL, SY, YU, ZA, ZM, ZW UG, ZM, ZW, AM, CY, CZ, DE, DK, PL, PT, RO, SE, GW, ML, MR, NE,			
SN, TD, TG PRIORITY APPLN. INFO.: OTHER SOURCE(S): CASREACT 141:411226; MARPAT 141:411226 IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of perindopril and its salts)								

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

L14 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 10 Sep 2004

AB A process for the preparation of perindopril and its salts involves reaction of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanyl chloride (I) or bromide with (2S)-indolinecarboxylic acid benzyl ester or its hexahydro derivative, followed by catalytic hydrogenation. Thus, perindopril benzyl ester was prepared by adding a slurry of 1.88 g I (preparation given) to a solution

of 1.6 g (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and triethylamine in CH2Cl2 at -10 to 15° over 25-30 min. Hydrogenation of the benzyl ester over 10% Pd-C afforded 1.3 g

perindopril.

ACCESSION NUMBER: 2004:740158 HCAPLUS

DOCUMENT NUMBER: 141:243833

TITLE: Process for preparation of perindopril and its

salts

INVENTOR(S): Datta, Debashish; Singh, Girij Pal; Godbole, Himanshu

Madhav; Siyan, Rajinder Singh

PATENT ASSIGNEE(S): Lupin Limited, India SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
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     WO 2004075889
                                         WO 2003-IN42
                         A1
                               20040910
                                                                  20030228
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                         CA 2003-2517205
     CA 2517205
                         AA
                               20040910
                                                                  20030228
     AU 2003224420
                         A1
                               20040917
                                           AU 2003-224420
                                                                  20030228
     EP 1603558
                         A1
                               20051214
                                           EP 2003-720846
                                                                  20030228
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE; HU, SK
PRIORITY APPLN. INFO.:
                                           WO 2003-IN42
                                                              W 20030228
OTHER SOURCE(S):
                        CASREACT 141:243833; MARPAT 141:243833
     82834-16-0P, Perindopril
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (preparation of perindopril and its salts)
RN
     82834-16-0 HCAPLUS
CN
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 27 May 2004

AB Perindopril was prepared by cyclization of (2S)-3-(2-bromophenyl)-2-[[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]propanoyl]amino]propanoic acid (I) or its esters in the presence of a Pd-based catalyst and a base [e.g., Pd2(dba)3, P(o-tolyl)3, and Cs2CO3], followed by catalytic hydrogenation. Intermediate I was prepared by coupling of N-[(S)-1-carbethoxybutyl]-Lalanine N-carboxyanhydride with (S)-2-bromophenylalanine.

ACCESSION NUMBER: 2004:427629 HCAPLUS

DOCUMENT NUMBER: 140:407114

TITLE: Method for synthesis of perindopril and its

> pharmaceutically-acceptable salts Dubuffet, Thierry; Langlois, Pascal

INVENTOR (S): PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 10 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND	DATE	APPLICATION NO.	DATE
A1 ·	20040526	EP 2003-292865	20031119
DE, DK	, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
LV, FI	, RO, MK,	CY, AL, TR, BG, CZ,	EE, HU, SK
A1	20050616	WO 2004-FR2937	20041118
AM, AT	, AU, AZ,	BA, BB, BG, BR, BW,	BY, BZ, CA, CH,
CU, CZ	, DE, DK,	DM, DZ, EC, EE, EG,	ES, FI, GB, GD,
	, -,,	22, 22, 22, 22, 22,	2, 31, 12, 111,
		EP 2003-292865	A 20031119
MARPAT			
			•
	cture): RO	CT (Reactant): SPN (S	Synthetic
	A1. , DE, DK, , LV, FI A1, AM, AT, , CU, CZ, , HR, HU, , LT, LU, , PG, PH, , TR, TT, , KE, LS, , KZ, MD, , FR, GB, , TR, BF , TG MARPAT dopril l manufac (Prepara	A1 20040526 , DE, DK, ES, FR, , LV, FI, RO, MK, A1 20050616 , AM, AT, AU, AZ, , CU, CZ, DE, DK, , HR, HU, ID, IL, , LT, LU, LV, MA, , PG, PH, PL, PT, , TR, TT, TZ, UA, , KE, LS, MW, MZ, , KZ, MD, RU, TJ, , FR, GB, GR, HU, , TR, BF, BJ, CF, , TG MARPAT 140:40713 dopril l manufacture); RG (Preparation); RA	EP 2003-292865 MARPAT 140:407114

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10/08/2006,10535187e.trn
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salts)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P, Perindopril erbumine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

IT 685141-30-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 685141-30-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 19 May 2004

2

GI

$$CO_2H$$
 O CH_3 CH_3 CH_3 CH_3 CH_3 CH_3 CH_3 CO_2Et CH_3 CH_3 CO_2Et CH_3

AB Perindopril (I), or a pharmaceutically acceptable salt thereof, may be prepared from a protected ester II (R = aralkyl, CH2Ph) via hydrogenolysis in the presence of a noble metal catalyst, such as Pd/charcoal, in the presence of a base. For example, when the base is tert-butylamine, it forms a pharmaceutically-acceptable addition salt with I, thus forming perindopril erbumine, I tert-butylamine salt. A monohydrate of I, or a pharmaceutically acceptable

salt thereof, is also claimed and may be prepared by hydrating I, or a pharmaceutically acceptable salt thereof, by way of addition of water or by drying in air. Perindopril erbumine monohydrate was prepared and studied by x-ray diffraction. Perindopril monohydrates may be used as angiotensin converting enzyme (ACE) inhibitors.

ACCESSION NUMBER: 2004:405692 HCAPLUS

DOCUMENT NUMBER: 140:407109

TITLE: Hydrogenolysis of benzyl ester of perindopril for

> preparing perindopril monohydrates for use as inhibitors of angiotensin converting enzyme (ACE)

INVENTOR(S): Rao, Dharmaraj Ramachandra; Kankan, Rajendra

Narayanrao

PATENT ASSIGNEE(S): Cipla Limited, India

SOURCE: Brit. UK Pat. Appl., 16 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                      KIND
                              DATE
                                        APPLICATION NO.
                                                                DATE
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     GB 2395195
                        A1
                              20040519 GB 2002-26885
                                                               20021118
     CA 2506587
                        AA
                              20040603
                                       CA 2003-2506587
                                                                20031118
     WO 2004046172
                        A1
                              20040603
                                        WO 2003-GB4981
                                                                20031118
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
            UG, US, UZ, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
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            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                              20040615 AU 2003-283588
     AU 2003283588
                        A1
                                                                20031118
                              20050824
     EP 1565485
                                        EP 2003-775565
                        A1
                                                                20031118
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            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003015703
                        A
                              20051025
                                        BR 2003-15703
                                                                20031118
     CN 1738830
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                              20060222
                                          CN 2003-80108700
                                                                20031118
    EP 1688427
                        A1
                              20060809
                                          EP 2006-76083
                                                                20031118
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK
     US 2006063941
                        A1 20060323
                                         US 2005-535187
                                                                20051031
PRIORITY APPLN. INFO.:
                                          GB 2002-26885
                                                             A 20021118
                                          EP 2003-775565
                                                             A3 20031118
                                          WO 2003-GB4981
                                                             W 20031118
OTHER SOURCE(S):
                       CASREACT 140:407109; MARPAT 140:407109
     690267-97-1P, Perindopril erbumine monohydrate
    RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic
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preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(crystal structure; preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN690267-97-1 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

with 2-methyl-2-propanamine (1:1), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

IT 82834-16-0P, Perindopril

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P, Perindopril erbumine
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 May 2004

AB A method for the synthesis of the title perindopril intermediate involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester or their salts with N-protected L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd.

ACCESSION NUMBER:

2004:405664 HCAPLUS

DOCUMENT NUMBER:

140:375492

TITLE:

Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid

derivatives and use in the synthesis of perindopril

INVENTOR(S):

Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

SOURCE:

Eur. Pat. Appl., 7 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA	CENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE		
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	EΡ		030																
		R:	ΑT,															PT,	
								RO,									SK		
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	WO	2005	0661	99		A1		2005	0721		WO 2	004-	FR31	67		2	0041	209	
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			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
			ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	ΥU,	ZA,	ZM,	ZW	
		RW:	BW,																
								RU,											
								GR,											
								BF,											
			-			TD,	-	,	,	,	,	,	,	,	,	- 2,	···,	,	
PRIO	RIT	APP	LN.	-	-	,					EP 2	003-	2930.	85		Δ 2	0031	210	
											WO 2						0041		
OTHE	R SC	URCE	:(s):			CAS	REAC	т 14	0:37							., 2	0041	200	
			6-0P								,								
			(Pr					ssif	ied)	: PR	EP (Pren	arat	ion)					
		(pre	para	tion	of	alan	vloc	tahv	droi	ndol	ecari	hoxv	lic	acid	der	ivs.	in	synthes	is of
			ndop:				, – • •											D / 1101100	15 01
RN	828	_	6-0		PLUS														
CN			le-2			lic a	acid	. 1-	[(28) -2-	[[(1:	S) - 1	_						
														, (2	S,3a	S,7a	S) -	(9CI)	

Absolute stereochemistry. Rotation (-).

(CA INDEX NAME)

L14 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 May 2004

AB A method for the synthesis of perindopril involves coupling of (2S) -indoline-2-carboxylic acid benzyl ester or (2S, 3aS, 7aS) octahydroindole-2-carboxylic acid benzyl ester with N-[(S)-1carbethoxybutyl]-L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd. Perindopril was converted into its tert-butylamine salt.

ACCESSION NUMBER:

2004:405663 HCAPLUS

DOCUMENT NUMBER:

140:375491

TITLE:

Method for the synthesis of perindopril and its

pharmaceutically-acceptable salts

INVENTOR (S):

Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

SOURCE:

Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

PRIO

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

					KIND DATE APPLICATION NO.										ATE		
EP	1420	029			A2 A3		2004	0519									
	R:				DE, LV,												PT,
		3121	85		A1 A1		2005	0721	· ·	AU 2	004-3	3121	85		2	0041	
,,,		AE, CN,	AG, CO,	AL, CR,	AM, CU, HR,	AT, CZ,	AU, DE,	AZ, DK,	BA, DM,	BB, DZ,	BG, EC,	BR, EE,	BW, EG,	BY, ES,	BZ, FI,	CA, GB,	CH, GD,
		LK, NO,	LR, NZ,	LS, OM,	LT, PG, TR,	LU, PH,	LV, PL,	MA, PT,	MD, RO,	MG, RU,	MK, SC,	MN, SD,	MW, SE,	MX, SG,	MZ, SK,	NA, SL,	NI, SY,
	RW:	BW, AZ, EE, RO,	GH, BY, ES, SE,	GM, KG, FI, SI,	KE, KZ, FR, SK,	LS, MD, GB, TR,	MW, RU, GR,	MZ, TJ, HU,	NA, TM, IE,	SD, AT, IS,	SL, BE, IT,	SZ, BG, LT,	TZ, CH, LU,	UG, CY, MC,	ZM, CZ, NL,	ZW, DE, PL,	AM, DK, PT,
ORITY ER SO	URCE	LN. :	INFO	.:		REAC'	Г 14		1	EP 20							

OTHE IT

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (synthesis of perindopril and its pharmaceutically-acceptable salts)

RN82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P, Perindopril erbumine

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10/08/2006,10535187e.trn
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Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

L14 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 19 May 2004 GI

$$Re \longrightarrow G$$
 CO_2R

AB A method for the synthesis of perindopril involves reaction of

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indolinecarboxylate derivs. I (R = H or a protective group, G = Cl, Br,
     OH, TsO, MeSO3 or CF3SO3) with (S)-PrCH(NH2)CO2Et (II), followed by
     catalytic hydrogenation. II was prepared by reaction of
     (S)-2-BrC6H4CH2CH(NH2)CO2R with (R)-MeCH(G)COC1 and intamol. coupling,
     e.g., in the presence of Pd2(dba)3, P(o-toly1)3, and Cs2CO3. Perindopril
     was converted into its tert-butylamine salt.
ACCESSION NUMBER:
                         2004:405662 HCAPLUS
DOCUMENT NUMBER:
                         140:375490
TITLE:
                         Method for the synthesis of perindopril and its
                         pharmaceutically-acceptable salts
INVENTOR(S):
                         Dubuffet, Thierry; Langlois, Pascal
PATENT ASSIGNEE(S):
                         Les Laboratoires Servier, Fr.
                         Eur. Pat. Appl., 8 pp.
SOURCE:
                         CODEN: EPXXDW
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         French
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                   DATE
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                                                                   _____
     EP 1420028
                                20040519
                         A2
                                          EP 2003-292864
                                                                   20031119
     EP 1420028
                                20040526
                         A3 ·
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     AU 2004295132
                                20050616 AU 2004-295132
                         A1
     CA 2546506
                         AA
                               .20050616
                                           CA 2004-2546506
     WO 2005054276
                                           WO 2004-FR2936
                         A1
                                20050616
                                                                   20041118
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, Fİ, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
             SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
            NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                           EP 2003-292864
                                                                A 20031119
                                           WO 2004-FR2936
                                                                   20041118
OTHER SOURCE(S):
                         CASREACT 140:375490; MARPAT 140:375490
     82834-16-0P, Perindopril 107133-36-8P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (synthesis of perindopril and its pharmaceutically-acceptable
        salts)
RN
     82834-16-0 HCAPLUS
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
CN
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1 ·

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

L14 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 01 Apr 2004

AB A method for the synthesis of perindopril involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an ester with N-[(S)-1-carbethoxybutyl]-L-alanine, followed by catalytic hydrogenation. I benzyl ester tosylate was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization. Perindopril was converted into

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its tert-butylamine salt.
ACCESSION NUMBER:
                        2004:266897 HCAPLUS
DOCUMENT NUMBER:
                        140:253917
TITLE:
                        Process for the synthesis of perindopril and its
                        pharmaceutically-acceptable salts
                        Dubuffet, Thierry; Langlois, Pascal
INVENTOR(S):
PATENT ASSIGNEE(S):
                        Les Laboratoires Servier, Fr.
SOURCE:
                        Eur. Pat. Appl., 9 pp.
                        CODEN: EPXXDW
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        French
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO.
                        KIND
                               DATE
                                         APPLICATION NO.
                                                                 DATE
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    EP 1403275
                         A1
                               20040331
                                        EP 2003-290485
                                                                 20030228
    EP 1403275
                         B1
                               20051019
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    AT 307139
                        E
                               20051115 AT 2003-290485
    ES 2250846
                        T3
                               20060416
                                         ES 2003-3290485
    AU 2004217599
                        A1
                               20040916
                                        AU 2004-217599
    WO 2004078107
                                          WO 2004-FR446
                        A2
                               20040916
                                                                 20040227
    WO 2004078107
                        A3
                               20041021
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
            BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
            MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
            GQ, GW, ML, MR, NE, SN, TD, TG
    CN 1753906
                         Α
                               20060329
                                           CN 2004-80005405
                                                                 20040227
    US 2006149081
                         A1
                               20060706
                                           US 2005-547131
                                                                 20050824
PRIORITY APPLN. INFO.:
                                           EP 2003-290485
                                                              A 20030228
                                           WO 2004-FR446
                                                             A 20040227
OTHER SOURCE(S):
                        MARPAT 140:253917
    82834-16-0P, Perindopril 107133-36-8P
    RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (synthesis of perindopril and pharmaceutically-acceptable salts
RN
    82834-16-0 HCAPLUS
CN
    1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 16 Jan 2004 GI

3

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Cl
CO2CH2Ph
                                II
                       NHBoc
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AB A method for the synthesis of perindopril and its tert-Bu amine salt is described. The steps are: coupling of hexahydroindolecarboxylate I with propionyl chloride II in CH2Cl2, followed by Boc deprotection with TFA and reaction with Et 2-oxopentanoate and hydrogenation over Pd/C. Addition of tert-butylamine to perindopril provides the salt.

ACCESSION NUMBER: 2004:36709 HCAPLUS

DOCUMENT NUMBER: 140:59939

TITLE: Method for synthesis of perindopril and its

pharmaceutically acceptable salts

INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.; Servier Lab

SOURCE: Eur. Pat. Appl., 7 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
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                                -----
                                                                   20030829
     EP 1380591
                         A1
                                20040114
                                           EP 2003-292132
     EP 1380591
                         B1
                                20051116
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     AT 310012
                         Ε
                                20051215
                                          AT 2003-292132
                                                                   20030829
     ES 2252633
                          Т3
                                20060516
                                            ES 2003-3292132
                                                                   20030829
     AU 2004270428
                          A1
                                20050317
                                           AU 2004-270428
                                                                   20040827
                                            WO 2004-FR2197
     WO 2005023842
                         A1
                                20050317
                                                                   20040827
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRIORITY APPLN. INFO.:
                                            EP 2003-292132
                                                                A 20030829
                                            WO 2004-FR2197
                                                                W 20040827
                         CASREACT 140:59939; MARPAT 140:59939
OTHER SOURCE(S):
     82834-16-0P, Perindopril 107133-36-8P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of perindopril and tert-butylamine salt)
     82834-16-0 HCAPLUS
     1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S, 3aS, 7aS)- (9CI)
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RN

CN

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 Jan 2004

AB A method for the synthesis of perindopril and its pharmaceutically-

acceptable salts involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid or its benzyl ester with R2-L-Ala-X (R2 is a protective group, X is halo), followed by deprotection, reaction with (R)-PrCH(G)CO2Et (G is Cl, Br, I, or tosyloxy), and catalytic hydrogenation. Addition of tert-butylamine to perindopril provides the salt.

ACCESSION NUMBER:

2004:36708 HCAPLUS

DOCUMENT NUMBER:

140:59938

TITLE:

Method for synthesis of perindopril and its

pharmaceutically acceptable salts

INVENTOR (S): Dubuffet, Thierry; Lecouve, Jean-Pierre Les Laboratoires Servier, Fr.

PATENT ASSIGNEE(S):

Eur. Pat. Appl., 9 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

RN

CN

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                        KIND
                               DATE
                                         APPLICATION NO.
                                                                DATE
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                                          -----
     EP 1380590
                         A1
                               20040114
                                        EP 2003-292131
                                                                 20030829
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     AU 2004270427
                         A1
                               20050317
                                          AU 2004-270427
                                                                 20040827
    WO 2005023841
                         A1
                               20050317
                                          WO 2004-FR2196
                                                                 20040827
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
PRIORITY APPLN. INFO.:
                                           EP 2003-292131
                                                              A 20030829
                                           WO 2004-FR2196
                                                              W
                                                                 20040827
OTHER SOURCE(S):
                        CASREACT 140:59938; MARPAT 140:59938
    82834-16-0P, Perindopril 107133-36-8P
    RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of perindopril and tert-butylamine salt)
    82834-16-0 HCAPLUS
    1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
     (CA INDEX NAME)
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Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 18 Dec 2003

GI

AB A method for the synthesis of perindopril (I) and its tert-Bu amine salt is described. The steps are: coupling of (hexahydro)indolecarboxylate II with propionyl chloride III in CH2Cl2, followed by Boc deprotection with TFA, reaction with Et 2-oxopentanoate under reductive conditions, and removal of benzyl ester by hydrogenation to give I. Addition of tert-Bu amine to I provides the salt.

ACCESSION NUMBER:

2003:985781 HCAPLUS

DOCUMENT NUMBER:

140:28049

TITLE:

Method for synthesis of perindopril and its pharmaceutically acceptable salts [2003/26] Dubuffet, Thierry; Lecouve, Jean-Pierre

INVENTOR(S):

Les Laboratoires Servier, Fr.

PATENT ASSIGNEE(S):

Eur. Pat. Appl., 8 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE APPLICATION NO.	DATE
EP 1371659 EP 1371659	A1 20031217 EP 2003-292133 B1 20051012	20030829
R: AT, BE, CH,	DE, DK, ES, FR, GB, GR, IT, LI, LU, I	
·	LV, FI, RO, MK, CY, AL, TR, BG, CZ, I E 20051015 AT 2003-292133	•
ES 2250853		
	A1 20050317 AU 2004-270429	
WO 2005023843	A1 20050317 WO 2004-FR2198	20040827
W: AE, AG, AL,	AM, AT, AU, AZ, BA, BB, BG, BR, BW, I	BY, BZ, CA, CH,
CN, CO, CR,	CU, CZ, DE, DK, DM, DZ, EC, EE, EG, I	ES, FI, GB, GD,
	HR, HU, ID, IL, IN, IS, JP, KE, KG, I	
	LT, LU, LV, MA, MD, MG, MK, MN, MW, M	
	PG, PH, PL, PT, RO, RU, SC, SD, SE, S	
The state of the s	TR, TT, TZ, UA, UG, US, UZ, VC, VN,	
	KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, U	
	KZ, MD, RU, TJ, TM, AT, BE, BG, CH, C	
	FR, GB, GR, HU, IE, IT, LU, MC, NL, I	
SI, SK, TR,	BF, BJ, CF, CG, CI, CM, GA, GN, GQ, C	GW, ML, MR, NE,
SN, TD, TG		
PRIORITY APPLN. INFO.:	EP 2003-292133	A 20030829
	WO 2004-FR2198	W 20040827
OTHER SOURCE(S):	CASREACT 140:28049; MARPAT 140:28049	

82834-16-0P

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perindopril and its tert-Bu amine salt)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

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NH<sub>2</sub>
H3C-C-CH3
           CH<sub>3</sub>
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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 05 Dec 2003

ΔR A method for the synthesis of perindopril and its pharmaceuticallyacceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carbethoxybutyl]-(S)-alanine with sulfinyl chlorides R1SOCl (R1 = imidazolyl, benimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril.

ACCESSION NUMBER: 2003:947713 HCAPLUS

DOCUMENT NUMBER: 139:381760

TITLE: Method for synthesis of perindopril and its

pharmaceutically acceptable salts

INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 8 pp. CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		APPLICATION NO.	
ED 1267061		202 ED 2002 201601	
		203 EP 2003-291601	20030630
EP 1367061			
		R, GB, GR, IT, LI, LU, NL,	
		IK, CY, AL, TR, BG, CZ, EE,	
AT 315043		215 AT 2003-291601	
ES 2256689	T3 20060'	716 ES 2003-3291601	
AU 2004253721	A1 20050:	13 AU 2004-253721	20040628
WO 2005003153	A1 20050:	AU 2004-253721 WO 2004-FR1637	20040628
		AZ, BA, BB, BG, BR, BW, BY,	
		OK, DM, DZ, EC, EE, EG, ES,	
		L, IN, IS, JP, KE, KG, KP,	
		MA, MD, MG, MK, MN, MW, MX,	• •
		PT, RO, RU, SC, SD, SE, SG,	
		JA, UG, US, UZ, VC, VN, YU,	
		MZ, NA, SD, SL, SZ, TZ, AUG,	
		J, TM, AT, BE, BG, CH, CY,	
		U, IE, IT, LU, MC, NL, PL,	
		CG, CI, CM, GA, GN, GQ, GW,	ML, MR, NE,
SN, TD, T			
		'12 CN 2004-80016014	20040628
PRIORITY APPLN. INFO.:	:	EP 2003-291601 A	1 20030630
		WO 2004-FR1637 V	V 20040628
OTHER SOURCE(S):	CASREACT 139	381760; MARPAT 139:381760	
IT 82834-16-0P, Peri			
	_	CDM (Complete areasonation	al DDED

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

Absolute stereochemistry. Rotation (-).

CRN 82834-16-0 CMF C19 H32 N2 O5

1

CM

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L14 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 20 Nov 2003 Perindopril and its pharmaceutically acceptable salts (e.g., tert-butylamine salt) are prepared by the cyclocondensation reaction of N-[(S)-carboethoxy-1-butyl]-(S)-alanine with a carbonyl compound X1COX2 (X1, X2 = leaving group; e.g., 1,1'-carbonyldiimidazole) to give Et (2S) -2-[(4S)-4-Methyl-2,5-dioxo-1,3-oxazolidin-3-yl]pentanoate which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid in the presence of an acid (e.g., hydrochloric acid) to give (2S)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]-2,3,4,5,6,7hexahydro-1H-indole-2-carboxylic acid which is hydrogenated with a 10% Pt/C catalyst to give perindopril which is then salified with tert-butylamine to give perindopril tert-butylammonium salt. ACCESSION NUMBER: 2003:909172 HCAPLUS DOCUMENT NUMBER: 139:396166 TITLE: Method for synthesis of perindopril and its pharmaceutically acceptable salts INVENTOR(S): Dubuffet, Thierry; Lecouve, Jean-Pierre PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr. SOURCE: Eur. Pat. Appl., 8 pp. CODEN: EPXXDW DOCUMENT TYPE: Patent LANGUAGE: French FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ----------EP 1362864 A1 20031119 EP 2003-291600 20030630 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK AU 2004255899 A1 20050120 AU 2004-255899 20040628 WO 2005005461 **A2** 20050120 WO 2004-FR1638 20040628 WO 2005005461 **A3** 20050331 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG CN 1805972 20060719 CN 2004-80016324 Α 20040628 US 2006148884 A1 20060706 US 2005-562950 20051223 PRIORITY APPLN. INFO.: EP 2003-291600 Α 20030630 WO 2004-FR1638 20040628 OTHER SOURCE(S): CASREACT 139:396166; MARPAT 139:396166 82834-16-0P, Perindopril RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (method for synthesis of perindopril and its pharmaceutically acceptable salts) RN82834-16-0 HCAPLUS CN1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

$$^{\mathrm{NH_2}}_{|}_{\mathrm{H_3C-C-CH_3}}_{|}_{|}_{\mathrm{CH_3}}$$

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

Young, Shawquia, Page 60

2

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 23 Oct 2003

The L-arginine salt of perindopril, which has increased storage AB stability over the corresponding tert-butylamine salt, is

prepared, and its use for the treatment of hypertension and cardiac

insufficiencyclaimed.

ACCESSION NUMBER: 2003:832150 HCAPLUS

DOCUMENT NUMBER: 139:307680

TITLE: Preparation of the L-arginine salt of

perindopril and its use as an ACE inhibitor

INVENTOR(S): Damien, Gerard; Lefoulon, Francois; Marchand, Bernard

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 5 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.					KIND DATE A1 20031022		APPLICATION NO.						DATE			
	13548 13548						2003 2004	1022 0714	1	EP	2003-	2903	83		2	0030	217
	R:	AT, IE,	BE, SI,	CH, LT,	DE, LV,	DK, FI,	ES, RO,	FR, MK,	GB, CY,	AL	, IT,	BG,	CZ,	EE,	HU,	MC, SK	PT,
	2838				A 1		2003	1024		FR	2002-	4847			2	0020	418
	2838				B1		2004										
WO	2003	0870	50°		A2		2003	1023	1	WO	2003-	FR50	7		2	0030	217
WO	2003						2004										
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB	, BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK	, SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
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	RW:										, TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
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											, NL,						
											, ML,						,
AU	20032	22292	21		A1		2003:	1027	- 7	AU :	2003-	22292	21		2	0030	217
AT	27103	36			E		2004	0715	7	AT :	2003-	29038	33		2	0030	217
	13548				E T		2004	1029]	PT :	2003-	29038	33		2	0030	217
ES	2224	92			T3		2005	0301	1	ES :	2003-	32903	383		2	0030	217
ZA	20030	00139	95		A		2003	0902	-	ZA :	2003 - : 2003 - : 2003 - : 2003 - :	1395			2	0030	220
	2003				A1		2003	1023	ī	US :	2003-	37186	55		2	0030	
US	66964	181			B2		2004								_		
	20030						2003:			NO :	2003-	849			2	0030	224
	20032				A1		2003				2003-:					0030	
	5244		_		A		2004				2003-					0030	
					_		2003:		(CN	2003-	10714	18		2	0030	
BR	20030	00070	9		Α		2004		ì	BR '	2003-: 2003-: 2003-:	709	• 0		2	0030	
	20033		93		A2		2003			TD '	2003-	, 0 2 8 3 2 5 (n		2	0030	
	37374				B2		2006		`		2005	0323	,			0030	323
· CA					AA		2003		(מר.	2003-:	24238	225		2	0030	403
	24238	-			C		2005		`	CA.	2005-	- 123(ب ت ر		2	0030	-03
	10573				A1		2005		ī	HK .	2004-:	10019	3 9		ว	0040	110
PRIORITY			NFO		A.		_005	-717			2004 2002 - 4			1		0020	
				• •							2002-1 2003-1					0030	
									•		2005-	LAJU I	•	,	, 2	0030	41

IT 612548-45-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor)

RN 612548-45-5 HCAPLUS

CN L-Arginine, mono[(2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate] (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 74-79-3 CMF C6 H14 N4 O2

Absolute stereochemistry.

REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 02 Oct 2003

AB (2S)-indoline-2-carboxylic acid, an intermediate used in the synthesis of perindopril, was prepared by resolution of racemic indoline-2-carboxylic acid by reaction with (R)- α -methylbenzylamine. In an example,

(2S)-indoline-2-carboxylic acid was obtained with enantiomeric purity > 99.5 %.

ACCESSION NUMBER:

2003:771360 HCAPLUS

DOCUMENT NUMBER:

139:277168

TITLE:

Method for the synthesis of (2S)-indoline-2-carboxylic

acid for use in the synthesis of perindopril

INVENTOR(S):

Souvie, Jean-Claude; Lecouve, Jean-Pierre

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

SOURCE: Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	PATENT NO.					KIND				APPL	ICAT	ION I	NO.		D	ATE	
						-									-		
EP	1348	684			A1		2003	1001		EP 2	003-	2908	79		2	00304	109
EP	1348	684			B1		2006	0308									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
							RO,										•
AT	3196	-	•		E		•			•	•				•		109
AU	2004	2302	94		A 1												
	2521				AA												
WO	2004	0920	95		A1										-		
							AU,										
							DE,										
		-					ID,		•	•	•	•		•			•
							LV,										
							PL,					-	-	-	-	-	-
		•			•		TZ,	•				•	•	•	•	•	
	DW.						MW,							-			
	1011.					-	TJ,			-	-	•	•		•		•
				-	-	-	-	•	-	-	•	•		•	•	•	
		•	-	-	•		HU,			-			•	•	•	•	•
				Dr,	ъυ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	Gw,	МЦ,	MR,	NE,	SN,
חח	2004	TD,			70		2006	0477		nn 2	004	0005			•	2040	
	2004						2006								_	00404	
	1768				A		2006									00404	
	2005				Α		2005	1109			005-					0051	
PRIORIT	Y APP	LN.	INFO	. :							003-		_	-		00304	
									,	WO 2	004-	FR85	7	Ī	N 20	00404	107

IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
 (synthesis of (2S)-indoline-2-carboxylic acid via resolution as
 intermediate in synthesis of perindopril)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
L14
ED
     Entered STN: 08 Aug 2003
AB
     The invention relates to 1-[2(S)-[1(S)-(ethoxycarbonyl)butylamino]propiony
     1]-(3aS,7aS)octahydroindole-2(S)-carboxylic acid (perindopril) and its
     tert-butylamine salt, free of contaminants derivable from
     dicyclohexylcarbodiimide, and a process for their synthesis.
     invention also relates to N-[1-(ethoxycarbonyl)butyl]-N-
     (alkoxycarbonyl) alanine intermediates used in the synthesis of
     perindopril, a known ACE inhibitor. Thus, N-[1-(ethoxycarbonyl)butyl]-N-
     (ethoxycarbonyl)alanine, prepared by ethoxycarbonylation of
     N-[1-(ethoxycarbonyl)butyl]alanine, was treated with thionyl chloride in
     CH2Cl2 and acylated by perhydroindole-2-carboxylic acid in THF at reflux
     for 4-4.5 h. The product was treated with tert-butylamine to afford 55%
     perindopril eburmine.
                         2003:609507 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         139:149930
TITLE:
                         Process for the preparation of high purity perindopril
                         and intermediates useful in its synthesis
INVENTOR (S):
                         Simig, Gyula; Mezei, Tibor; Porcs-Makkay, Marta;
                         Mandi, Attila
PATENT ASSIGNEE(S):
                         Les Laboratoires Servier, Fr.
SOURCE:
                         Eur. Pat. Appl., 12 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                         KIND
                               DATE
                                           APPLICATION NO.
                                                                   DATE
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                                20030806
                                          EP 2002-290206
                         A1
                                                                   20020130
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     CA 2474003
                         AΑ
                                20030807
                                           CA 2003-2474003
                                                                   20030129
     WO 2003064388
                         A2
                                20030807
                                           WO 2003-IB691
                                                                   20030129
     WO 2003064388
                         Α3
                                20040205
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    EE 200400107
                         Α
                                20041015
                                          EE 2004-107
                                                                   20030129
    BR 2003007293
                         Α
                                20041221
                                           BR 2003-7293
                                                                   20030129
     CN 1622936
                         Α
                                20050601
                                           CN 2003-802714
                                                                   20030129
    US 2005119492
                         A1
                                20050602
                                           US 2003-503272
                                                                   20030129
    JP 2005521667
                         T2
                                20050721
                                           JP 2003-564011
                                                                   20030129
    NO 2004003472
                         Α
                                20040820
                                           NO 2004-3472
                                                                   20040820
    BG 108858
                                20050531
                                           BG 2004-108858
                         Α
                                                                   20040827
PRIORITY APPLN. INFO.:
                                           EP 2002-290206
                                                               A 20020130
                                           WO 2003-IB691
                                                               W 20030129
OTHER SOURCE(S):
                        MARPAT 139:149930
     82834-16-0P, Perindopril 107133-36-8P, Perindopril
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RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)

(process for preparation of high purity perindopril and intermediates useful in its synthesis)
RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L14
    ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN
ED
     Entered STN: 27 Jun 2003
     Perindopril and its pharmaceutically-acceptable salts were
     prepared from 2,7-oxepanedione by a multistep procedure, i.e., reaction with
     (R)-XCH2CH(NHBoc)CO2CH2Ph (X is Br or iodo; Boc is tert-butoxycarbonyl),
     cyclization of deprotected 2-amino-4-oxononanedioic acid derivative,
     Ti-catalyzed coupling to form the indole ring system; reaction with
     N-[(S)-1-carbethoxybutyl]-(S)-alanine, and catalytic hydrogenation.
                                                                         In an
     example, perindopril was obtained with enantiomeric purity 99%.
ACCESSION NUMBER:
                        2003:488613 HCAPLUS
                        139:22503
DOCUMENT NUMBER:
TITLE:
                        Method for the synthesis of perindopril and its
                        pharmaceutically-acceptable salts
                        Dubuffet, Thierry; Lecouve, Jean-pierre
INVENTOR(S):
PATENT ASSIGNEE(S):
                        Les Laboratoires Servier, Fr.
SOURCE:
                        Eur. Pat. Appl., 9 pp.
                        CODEN: EPXXDW
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        French
FAMILY ACC. NUM. COUNT:
                        1
PATENT INFORMATION:
     PATENT NO.
                                         APPLICATION NO.
                        KIND
                               DATE
                                                                 DATE
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    EP 1321471
                        A1
                               20030625
                                        EP 2003-290605
                                                                20030312
    EP 1321471
                        B1
                               20050504
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    AT 294814
                        E
                               20050515 AT 2003-290605
                                                                 20030312
    PT 1321471
                         Т
                               20050729
                                        PT 2003-290605
                                                                 20030312
    ES 2240919
                        Т3
                               20051016
                                        ES 2003-3290605
                                                                 20030312
    WO 2004083238
                        A1
                               20040930
                                         WO 2004-FR594
                                                                  20040312
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
            SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
            TD, TG
PRIORITY APPLN. INFO.:
                                           EP 2003-290605
                                                               A 20030312
OTHER SOURCE(S):
                        CASREACT 139:22503; MARPAT 139:22503
    82834-16-0P, Perindopril 107133-36-8P
    RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
        (method for synthesis of perindopril and its pharmaceutically-
       acceptable salts)
RN
    82834-16-0 HCAPLUS
CN
    1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-
     (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)
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Absolute stereochemistry. Rotation (-).

(CA INDEX NAME)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 31 Jan 2003

AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]pro pionyl]oc tahydro-1H-indole-2-carboxylic acid] or its analogs or salts were prepared by treating RcCH(CO2Ra)NHCHRbCO2H (Ra, Rb = C1-4 alkyl, Rc = C1-6alkyl) with X2C:O (X is a leaving group) to give a

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2,5-dioxooxazolidine, which reacts with octahydro-1H-indole-2-carboxylic
     acid or ester to give the desired product. In an example,
     N,N'-carbonyldiimidazole was added to a suspension of N-[(S)-1-
     carbethoxybutyl]-(S)-alanine in CH2Cl2 and the mixture kept at 0° for
           (2S, 3aS, 7aS) -octahydroindole-2-carboxylic acid was added at
     -5°C and the solution kept at this temperature for 1 h to give 80%
     perindopril (isolated as the tert-butylamine salt).
                        2003:77804 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                        138:107004
TITLE:
                        A process for the preparation of perindopril, its
                        analogs and salts using 2,5-dioxooxazolidine
                        intermediate compounds
INVENTOR (S):
                        Cid, Pau
PATENT ASSIGNEE(S):
                        Adir, Fr.
SOURCE:
                        Eur. Pat. Appl., 11 pp.
                        CODEN: EPXXDW
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                                         APPLICATION NO.
                       KIND DATE
                                                                DATE
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                                           -----
     EP 1279665
                         A2
                               20030129
                                         EP 2002-16262
                                                                  20020723
     EP 1279665
                               20030312
                         A3
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     WO 2003010142
                               20030206
                                          WO 2002-EP8223
                        A2
                                                                  20020723
     WO 2003010142
                         A3
                               20030828
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW-
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                               20040817
     BR 2002011422
                         Α
                                        BR 2002-11422
                                                                  20020723
     CN 1529694
                               20040915
                                           CN 2002-814322
                         Α
                                                                  20020723
     JP 2005501829
                         T2
                               20050120
                                           JP 2003-515501
                                                                  20020723
     ZA 2004000323
                               20050117
                                           ZA 2004-323
                         Α
                                                                  20040115
     US 2004248814
                                           US 2004-484672
                         A1
                               20041209
                                                                  20040712
PRIORITY APPLN. INFO.:
                                                              A 20010724
                                           EP 2001-500197
                                                              W 20020723
                                           WO 2002-EP8223
OTHER SOURCE(S):
                        MARPAT 138:107004
    82834-16-0P, Perindopril 107133-36-8P, Perindopril
     erbumine
     RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
     (Reactant or reagent)
        (process for preparation of perindopril using dioxooxazolidine intermediate)
     82834-16-0 HCAPLUS
ВN
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(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)

Absolute stereochemistry. Rotation (-).

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(CA INDEX NAME)

CN

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

L14 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 17 Aug 2001

AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]pro pionyl]octahydro-1H-indole-2-carboxylic acid] was prepared by coupling (2S,3aS,7aS)octahydroindole-2-carboxylic acid tosylate with N-[(S)-1-carbethoxybutyl]-(S)-alanine, followed by catalytic hydrogenation to remove the benzyl group. In an example, the coupling reaction was carried out in Et acetate in the presence of Et3N, 1-hydroxybenzotriazole

and dicyclohexylcarbodiimide at 30° for 3h to give 92% perindopril benzyl ester.

ACCESSION NUMBER:

2001:597957 HCAPLUS

DOCUMENT NUMBER:

135:167034

TITLE:

Method for synthesis of perindopril and its

pharmaceutically acceptable salts Langlois, Pascal; Turbe, Hugues

INVENTOR (S): PATENT ASSIGNEE(S): SOURCE:

Adir et Compagnie, Fr. PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.							DATE			APP:	LICAT	'ION	NO.		D	ATE	
		2001																
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB	, BG,	BR,	BY,	BZ,	CA,	CH,	CN,
												, ES,						
												, KP,						
												, мх,						
												TR,	-	-	-	-	-	•
				YU,						,		,,		,	,	,	,	,
		RW:	•	•	•		MW.	MZ.	SD.	SL.	SZ	, TZ,	UG.	ZW.	AT.	BE.	CH.	CY.
					-	-		-	-			, LU,		-	-			
												, <u> </u>						,
	FR	2807																406
		2807														_		100
	CA	2405	486			AA		2001	0816		CA	2001-	2405	486		2	0010	405
	AU	2405 2001	0484	70		A5		2001	0820		AU :	2001-	4847	0		2	0010	405
		1268																
												, IT,						
						-	FТ	PΩ	MK	CV	ΔT.	מידי	•	-		-	-	-
	BR	2001				-	,	2003	0624	,	BR :	, IR 2001-	9836			2	0010	405
	JP	2003	5318	25		Т2						2001-						
	NZ	5214	54			A		2004	0326		NZ	2001-	5214	54		2	0010	405
	EE	5214 2002	0057	5		A		2004	0415		EE :	2002-	575	-		2	0010	405
		2002										2002-						
		2003										2002-					0020	
		6835		_		B2		2004								_	0020	
		2002		0.8							NO '	2002-	4808			2	0021	004
		1072															0021	
PRIO									0,01			2000-						
					• •						WO .	2001-	FR10	26	-	W 2	0010	405
OTHER	R SC	URCE	(S):			CASI	REAC	T 13	5:16					_ •				
		334-1																
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RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(method for synthesis of perindopril)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 107133-36-8P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(method for synthesis of perindopril)

RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

REFERENCE COUNT:

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 01 Oct 1989

AB Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine. The title compound (I), useful as an antihypertensive (no data), is prepared, e.g., via N-acylation of perhydroindole derivative II (preparation given) with (S,S)-HO2CCHMeNHCHPrCO2Et (III). II.p-MeC6H4SO3H (preparation given) was condensed with III in EtOAc containing Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to give, after deprotection and treatment with Me3CNH2, I.Me3CNH2.

ACCESSION NUMBER: 1989:515749 HCAPLUS

DOCUMENT NUMBER: 111:115749

TITLE: Preparation of perindopril via acylation of

perhydroindolecarboxylate with N[(ethoxycarbonyl)butyl]alanine

INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard;

Remond, Georges

PATENT ASSIGNEE(S): ADIR, Fr.

SOURCE: Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT NO.			DATE	APPLICATION NO.		DATE
	308341		A1	19890322	EP 1988-402339		19880916
EP	308341		B1	19901212			
	R: AT,	BE, C	CH, DE, E	S, FR, GB,	GR, IT, LI, LU, NL, S	E	
FR	2620709		A1	19890324	FR 1987-12896		19870917
FR	2620709		B1	19900907			
CA	1336348		A1	19950718	CA 1988-577078		19880907
DK	8805151		A	19890318	DK 1988-5151		19880915
DK	171470		B1	19961111			
AU	8822362		A1	19890323	AU 1988-22362		19880916
AU	608363		B2	19910328			
JP	01110696		A2	19890427	JP 1988-232125		19880916
JP	05043717		B4	19930702			
ZA	8806932		A	19890530	ZA 1988-6932		19880916
US	4914214		A	19900403	US 1988-245446		19880916
AT	59047		É	19901215	AT 1988-402339		19880916
CA	1338015		A1	19960130	CA 1991-616239		19911128
PRIORIT	Y APPLN. 1	INFO.:	:		FR 1987-12896	A	19870917
					CA 1988-577078	A3	19880907
					EP 1988-402339	Α	19880916

OTHER SOURCE(S): MARPAT 111:115749

IT 107133-36-8P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, via acylation of perhydroindole derivative with

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10/08/2006,10535187e.trn
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N-[(ethoxycarbonyl)butyl]alanine) RN 107133-36-8 HCAPLUS CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME) CM CRN 82834-16-0 CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

CM 2

CRN 75-64-9 CMF C4 H11 N

IT

82834-16-0P, Perindopril RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine) RN82834-16-0 HCAPLUS CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 24 Dec 1988

GI

AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

ACCESSION NUMBER:

1988:631529 HCAPLUS

DOCUMENT NUMBER:

109:231529

TITLE:

Synthesis of S9490-3 [U-14C-cyclohexyl]

1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic

acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-

(carboxybutyl) amino] -1-oxopropyl] -2S, 3aS, 7aS) -

perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino] S9490-3 and [(3,4-3H-

)butylamino]S9780

AUTHOR (S):

Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin,

B.; Laubie, M.

CORPORATE SOURCE:

CEN Saclay, Gif sur Yvette, 91191, Fr.

SOURCE:

Journal of Labelled Compounds and Radiopharmaceuticals

(1988), 25(5), 553-68

CODEN: JLCRD4; ISSN: 0362-4803

DOCUMENT TYPE:

Journal

LANGUAGE:

French

OTHER SOURCE(S):

CASREACT 109:231529

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10/08/2006,10535187e.trn
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117770-49-7P 117770-64-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of) RN 117770-49-7 HCAPLUS 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-CNoxopropyl]octahydro-, labeled with carbon-14, [2S- $[1[R*(R*)], 2\alpha, 3a\alpha, 7a\beta]]$ -, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME) CM 1 CRN 117770-48-6 CMF C19 H32 N2 O5 CIL XC-14

Absolute stereochemistry.

CM 2

CRN 75-64-9 CMF C4 H11 N

RN 117770-64-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl-3,4-t2]amino]1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 23 Jan 1988 GI

CO2R6
COCHMENHCH
$$-B$$
 $-NHSO_2$
 $-NH$
 $-CO_2H$
 D-SO2NR1-B-CH(COR6)-E-CHR7-CO-A-COR8 [I; A = heterocycle residue, e.g., 1,2-pyrrolidinediyl, 1,2-perhydroindolediyl; B = (substituted) hydrocarbon residue, e.g., (CH2)4; D-substituted S,S-dioxo-3,4-dihydro-1,2,4-benzothiadiazin-7-yl; E = NH, O, S, CH2], e.g., II [R6 = H, B = (CH2)4, X = CH2Cl] (III), useful for reducing intraocular pressure, are prepared Dipeptide II (R6 = Et, B = p-CH2OCH2C6H4CH2, X = CH2CH2Ph) was prepared in many steps via alkylation of indole derivative IV with alanine derivative V followed by hydrogenolysis. An antiglaucoma composition (1 mL) (adjusted to pH 7.4 with 1N NaOH) for topical use contained III 10.0, NaH2PO4 10.4, Na2HPO4 2.4, chlorobutanol 5.0, hydroxypropyl methylcellulose 5.0 g, and water.

ACCESSION NUMBER:

1988:22286 HCAPLUS

DOCUMENT NUMBER:

108:22286

TITLE: Preparation of peptides as antiglaucoma agents

INVENTOR(S): Andrews, David R.; Gaeta, Federico C. A.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: U.S., 15 pp. Cont.-in-part of U.S. 4,556,655.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4634698	Α	19870106	US 1985-721015	19850408
US 4556655	Α	19851203	US 1984-653186	19840924
US 4826816	A	19890502	US 1985-784000	19851004
US 4885293	Α	19891205	US 1986-892003	19860730
US 5015641	Α	19910514	US 1989-349369	19890509
PRIORITY APPLN. INFO.:			US 1984-653186 A	2 19840924
			US 1985-721015 A	2 19850408
			US 1985-784000 A	2 19851004
			US 1986-892003 A	3 19860730

OTHER SOURCE(S): CASREACT 108:22286

IT 109854-18-4P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as antiglaucoma agent)

RN 109854-18-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[6-chloro-3-(chloromethyl)-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 19 Sep 1987

AB The title compds. useful in treatment of hypertension and glaucoma (no data) were prepared 1-[2-(S)-[[1-(S)-Carboxy-2-[4-[[[6-chloro-3,4-dihydro-3-(2-phenylethyl)-2H-1,2,4-benzothiadiazin-7-yl]sulfonylamino]methyl]pheny lmethoxy]ethyl]amino]-1-oxopropyl]-(2S,3α,7aα)-octahydro-1H-indole-2-carboxylic acid S,S-dioxide prepared in 8 steps from N-tert-butoxycarbonyl-L-serine, was used in formulation of a capsule,

tablet, and injectable solution

ACCESSION NUMBER:

1987:497126 HCAPLUS

DOCUMENT NUMBER:

107:97126

TITLE:

Dipeptide derivatives containing sulfoamide group as antihypertensives having both diuretic and angiotensin

converting enzyme inhibitory activity

INVENTOR(S):

Andrews, David R.; Gaeta, Federico C. A.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE: U.S., 16 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

	PA'	TENT	NO.			KINI)	DATE		AP	PLICATION	NO.		DATE
	US	4556 4634	655			A	-	1985			1984-6531			19840924
								1987	0106		1985-7210			19850408
	WO	8601				A 1		1986	0327	WO	1985-US17	778		19850919
			ΑU,											
											L, SE			
	ΑU	8549	639						0408	AU	1985-4963	39		19850919
		5813				B2		1989	0216					
	ΕP	1958	17			A1		1986	1001	EP	1985-9050	15		19850919
	ΕP	1958	17			B1		1989	1018					
		R:	AΤ,	BE,	CH,	DE,	FR	, GB,	IT,	LI, L	U, NL, SE			
	JP	6250				T2		1987	0129	JP	1985-5044	153		19850919
	ΑT	4739	9			E		1989	1115	ΑT	1985-9050	15		19850919
	ZA	8507	358			Α		1986	0528	ZA	1985-7358	3		19850924
		7648				A1		1990	0209	IL	1985-7648	34		19850924
	CA	1278	150			A1		1990	1218	CA	1985-4914	47		19850924
	US	4826				Α		1989		US	1985-7840	00		19851004
	DK	8602	416			A		1986	0523	DK	1986-2416	5		19860523
	US	4885	293			Α		1986 1989	1205	US	1986-8920	003		19860730
	US	5015				Α					1989-3493	869		19890509
PRIO	RITY	APP	LN.	INFO	. :					US	1984-6531	.86	A2	19840924
										US	1985-7210	15	A2	19850408
										EP	1985-9050	15	Α	19850919
										WO	1985-US17	778 [.]	Α	19850919
											1985-7840			
								•		US	1986-8920	003	A3	19860730

OTHER SOURCE(S): CASREACT 107:97126; MARPAT 107:97126

IT 109854-18-4P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of, as drug)

RN 109854-18-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[6-chloro-3-(chloromethyl)-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2006 ACS on STN ED Entered STN: 13 Jul 1986

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
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AB The title compds. [I, II, X = Cl, CF3; Y = (CH2)aCHONR5 or (CH2)bNR5CO; Z= (CH2)bCONR5 or (CH2)cNR5CO; B = Q-Q4; R1 = H, alky1; R2, R5 = H, alky1, Ph, phenylalkyl; R3, R4 = H, (substituted) alkyl, Ph or R3R4 may form a ring; R6, R8 = OH, (substituted) alkoxy, etc.; R7 = H, (substituted) alkyl; a = 0-8; b = 1-8; c = 2-8; m = 1-4; n = 0, 1; p, q = 1, 0, 2] and their pharmaceutically acceptable salts, useful as antihypertensives (no data), were prepared Thus, (2S)-[(benzyloxy)carbonyl]-S,S-perhydroindole was acylated with N-[(5S)-(ethoxycarbonyl)-5-(1Scarboxyethylamino)pentyl]-6-chloro-3,4-dihydro-1,1-dioxo-7-sulfamoyl-1,2,4benzothiadiazin-3-yl]acetamide hydrochloride in DMF containing N-hydroxybenzotriazole hydrate and 1-[3-(dimethylamino)propyl]-3ethylcarbodiimide-HCl at 0° to give, after deprotection of the intermediate, 1-[N-[(1S)-(ethoxycarbonyl)-5-[2-(6-chloro-3,4-dihydro-1,1dioxo-7-sulfamoyl-1,2,4-benzothiadiazin-3-yl)acetamido]pentyl]-(S)-alanyl]cis, syn-octahydroindole-(2S)-carboxylic acid. The prepared compds. are useful for treatment of congestive heart failure and glaucoma and had diuretic activity (no data).

ACCESSION NUMBER: 1986:406825 HCAPLUS

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105:6825

TITLE:

Benzothiadiazinyl and quinazolinyl substituted

carboxylalkyl dipeptides useful as antihypertensive

INVENTOR(S):

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Paul E.

PATENT ASSIGNEE(S):

Schering Corp., USA

SOURCE:

U.S., 12 pp.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4559340	Α	19851217	US 1983-555311	19831125
US 4616012	A	19861007	US 1985-797104	19851112
US 4778795	Α	19881018	US 1986-903545	19860903
US 4906635	Α	19900306	US 1988-220183	19880718
US 5017567	Α	19910521	US 1990-460425	19900103
PRIORITY APPLN. INFO.:			US 1983-555311	A2 19831125
			US 1985-797104	A3 19851111
•			US 1986-903545	A3 19860903
			US 1988-220183	A3 19880718

IT 102605-78-7P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of)

RN 102605-78-7 HCAPLUS

1H-Indole-2-carboxylic acid, 1-[2-[[4-[[[7-(aminosulfonyl)-6-chloro-3,4-CN dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]acetyl]amino]-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, hydrobromide (9CI) (CA INDEX NAME)

•x HBr

IT 102605-60-7P 102605-62-9P 102743-99-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as antihypertensive)

RN 102605-60-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]acetyl]amino]-1-(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

RN 102605-62-9 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[4-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]acetyl]amino]-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, hydrochloride (9CI) (CA INDEX NAME)

•x HCl

RN 102743-99-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[5-[[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-2-yl]acetyl]amino]-1(ethoxycarbonyl)pentyl]amino]-1-oxopropyl]octahydro-, [2S[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

=> log h COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 194.08 1069.31